

Inventors: Seidman and Théorêt
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Please amend the claims as follows:

1. (Amended) A method of optimizing therapeutic efficacy [of 6-mercaptopurine drug] for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) administering a [6-mercaptopurine] drug to a subject having said immune-mediated gastrointestinal disorder, wherein said drug provides 6-thioguanine to said subject; and

(b) determining a level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein a level of 6-thioguanine less than a level corresponding to about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of [6-mercaptopurine] said drug subsequently administered to said subject and

wherein a level of 6-thioguanine greater than a level corresponding to about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject.

7. (Amended) A method of reducing toxicity associated with [6-mercaptopurine drug] treatment of an immune-mediated gastrointestinal disorder, comprising:

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(a) administering a [6-mercaptopurine] drug to a subject having said immune-mediated gastrointestinal disorder, wherein said drug provides 6-thioguanine to said subject; [and]

(b) determining a level of [a 6-mercaptopurine metabolite] 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder[,]; and

(c) determining a level of 6-methyl-mercaptopurine in said subject having said immune-mediated gastrointestinal disorder,

wherein a level of [said 6-mercaptopurine metabolite] 6-thioguanine greater than [a predetermined toxic level of said 6-mercaptopurine metabolite] about 400 pmol per 8×10^8 red blood cells or a level of 6-methyl-mercaptopurine greater than about 7000 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby reducing toxicity associated with [6-mercaptopurine] said drug treatment of said immune-mediated gastrointestinal disorder.

B3 11/13. (Amended) The method of claim [11] 7, wherein said toxicity associated with [6-mercaptopurine] said drug treatment is hematologic toxicity.

B4 12/16. (Amended) The method of claim [14] 7, wherein said toxicity associated with [6-mercaptopurine] said drug treatment is hepatic toxicity.

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17. (Amended) The method of claim 7, wherein said level of [6-mercaptopurine metabolite] 6-thioguanine and said level of 6-methyl-mercaptopurine each is determined in red blood cells.

19. (Amended) A method of optimizing therapeutic efficacy and reducing toxicity associated with [6-mercaptopurine drug] treatment of an immune-mediated gastrointestinal disorder, comprising:

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(a) administering a [6-mercaptopurine] drug to a subject having said immune-mediated gastrointestinal disorder, wherein said drug provides 6-thioguanine to said subject;

(b) determining a level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder; and

(c) determining a level of 6-methyl-mercaptopurine in said subject having said immune-mediated gastrointestinal disorder,

wherein a level of 6-thioguanine less than [a predetermined minimal therapeutic level] about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby increasing therapeutic efficacy,

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wherein a level of 6-thioguanine greater than [a predetermined toxic level of 6-thioguanine] about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby reducing toxicity associated with [6-mercaptopurine] said drug treatment of said immune-mediated gastrointestinal disorder, and

wherein a level of 6-methyl-mercaptopurine greater than [a predetermined toxic level of 6-methyl-mercaptopurine] about 7000 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby reducing toxicity associated with [6-mercaptopurine] said drug treatment of said immune-mediated gastrointestinal disorder.

In claim 29, line 2, please delete "6-mercaptopurine" and insert therefor --said--.

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30. (Amended) A method of optimizing therapeutic efficacy of [6-mercaptopurine drug] treatment of a non-IBD autoimmune disease, comprising:

(a) administering a [6-mercaptopurine] drug to a subject having said non-IBD autoimmune disease, wherein said drug provides 6-thioguanine to said subject; and

(b) determining a level of 6-thioguanine in said subject having said non-IBD autoimmune disease,

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wherein a level of 6-thioguanine less than [a minimal therapeutic level] about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of [6-mercaptopurine] said drug subsequently administered to said subject and

wherein a level of 6-thioguanine greater than [a level corresponding to a predetermined toxic level] about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject.

In claim 33, line 2, please delete "6-mercaptopurine metabolite" and insert therefor --6-thioguanine--.

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35. (Amended) A method of optimizing therapeutic efficacy and reducing toxicity associated with [6-mercaptopurine drug] treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) administering a [6-mercaptopurine] drug to a subject having said immune-mediated gastrointestinal disorder, wherein said drug provides 6-thioguanine to said subject; [and]

(b) determining a level of [a 6-mercaptopurine metabolite] 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder[,]; and

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(c) determining a level of 6-methyl-mercaptopurine in said subject having said immune-mediated gastrointestinal disorder,

wherein a level of [said 6-mercaptopurine metabolite] 6-thioguanine less than [a predetermined minimal therapeutic level] about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby increasing therapeutic efficacy, and

wherein a level of [said 6-mercaptopurine metabolite] 6-thioguanine greater than [a predetermined toxic level of said 6-mercaptopurine metabolite] about 400 pmol per 8×10^8 red blood cells or a level of 6-methyl-mercaptopurine greater than about 7000 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of [6-mercaptopurine] said drug subsequently administered to said subject, thereby reducing toxicity associated with [6-mercaptopurine] said drug treatment of said immune-mediated gastrointestinal disorder.

38 29/44. (Amended) The method of claim 25/38, wherein said level of [said 6-mercaptopurine metabolite] 6-thioguanine and said level of 6-methyl-mercaptopurine each is determined in red blood cells.

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In claim 46, line 2, please delete "6-mercaptopurine" and insert therefor --said--.

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Please add the following new claims.

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~~47~~. (New) The method of claim 1, wherein said drug is selected from the group consisting of 6-mercaptopurine, azathioprine, 6-thioguanine, and 6-methylmercaptopurine riboside.

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~~48~~. (New) The method of claim 7, wherein said drug is selected from the group consisting of 6-mercaptopurine, azathioprine, 6-thioguanine, and 6-methylmercaptopurine riboside.

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~~49~~. (New) The method of claim ~~15~~
~~19~~, wherein said drug is selected from the group consisting of 6-mercaptopurine, azathioprine, 6-thioguanine, and 6-methylmercaptopurine riboside.

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~~50~~. (New) The method of claim ~~22~~
~~30~~, wherein said drug is selected from the group consisting of 6-mercaptopurine, azathioprine, 6-thioguanine, and 6-methylmercaptopurine riboside.

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~~51~~. (New) The method of claim ~~25~~
~~35~~, wherein said drug is selected from the group consisting of 6-mercaptopurine, azathioprine, 6-thioguanine, and 6-methylmercaptopurine riboside.

52. (New) A method of optimizing therapeutic efficacy of treatment of a non-IBD autoimmune disease, comprising:

(a) administering a drug to a subject having said non-IBD autoimmune disease, wherein said drug provides 6-thioguanine to said subject;

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(b) determining a level of 6-thioguanine in said subject having said non-IBD autoimmune disease; and

(c) determining a level of 6-methyl-mercaptopurine in said subject having said non-IBD autoimmune disease,

wherein a level of 6-thioguanine less than about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein a level of 6-thioguanine greater than about 400 pmol per 8×10^8 red blood cells or a level of 6-methyl-mercaptopurine greater than about 7000 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject, thereby reducing toxicity associated with said drug treatment of said non-IBD autoimmune disease.

53. (New) The method of claim 52, wherein said level of 6-thioguanine and said level of 6-methyl-mercaptopurine each is determined in red blood cells.

54. (New) The method of claim 53, wherein said level is determined using high pressure liquid chromatography.--

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